

Food and Drug Administration, HHS

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that are needed to support marketing approval. Based on these recommendations, a cost estimate should be prepared.

(5) A statement of and justification for production and marketing costs that the sponsor has incurred in the past and expects to incur during the first 7 years that the drug is marketed.

(6) An estimate of and justification for the expected revenues from sales of the drug in the United States during its first 7 years of marketing. The justification should assume that the total market for the drug is equal to the prevalence of the disease or condition that the drug will be used to treat. The justification should include:

(i) An estimate of the expected market share of the drug in each of the first 7 years that it is marketed, together with an explanation of the basis for that estimate;

(ii) A projection of and justification for the price at which the drug will be sold; and

(iii) Comparisons with sales of similarly situated drugs, where available.

(7) The name of each country where the drug has already been approved for marketing for any indication, the dates of approval, the indication for which the drug is approved, and the annual sales and number of prescriptions in each country since the first approval date.

(8) A report of an independent certified public accountant in accordance with Statement on Standards for Attestation established by the American Institute of Certified Public Accountants on agreed upon procedures performed with respect to the data estimates and justifications submitted pursuant to this section. Cost data shall be determined in accordance with generally accepted accounting principles.

(d) A sponsor that is requesting orphan-drug designation for a drug designed to treat a disease or condition that affects 200,000 or more persons shall, at FDA's request, allow FDA or FDA-designated personnel to examine at reasonable times and in a reasonable manner all relevant financial records

and sales data of the sponsor and manufacturer.

[57 FR 62085, Dec. 29, 1992, as amended at 78 FR 35133, June 12, 2013]

§ 316.22 Permanent-resident agent for foreign sponsor.

Every foreign sponsor that seeks orphan-drug designation shall name a permanent resident of the United States as the sponsor's agent upon whom service of all processes, notices, orders, decisions, requirements, and other communications may be made on behalf of the sponsor. Notifications of changes in such agents or changes of address of agents should preferably be provided in advance, but not later than 60 days after the effective date of such changes. The permanent-resident agent may be an individual, firm, or domestic corporation and may represent any number of sponsors. The name of the permanent-resident agent, address, telephone number, and email address shall be provided to: Office of Orphan Products Development, Food and Drug Administration, Bldg. 32, rm. 5271, 10903 New Hampshire Ave., Silver Spring, MD 20993.

[78 FR 35133, June 12, 2013]

§ 316.23 Timing of requests for orphan-drug designation; designation of already approved drugs.

(a) A sponsor may request orphan-drug designation at any time in its drug development process prior to the time that sponsor submits a marketing application for the drug for the same rare disease or condition.

(b) A sponsor may request orphan-drug designation of an already approved drug for an unapproved use without regard to whether the prior marketing approval was for a rare disease or condition.

[78 FR 35133, June 12, 2013]

§ 316.24 Deficiency letters and granting orphan-drug designation.

(a) FDA will send a deficiency letter to the sponsor if the request for orphan-drug designation lacks information required under §§ 316.20 and 316.21, or contains inaccurate or incomplete

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information. FDA may consider a designation request voluntarily withdrawn if the sponsor fails to respond to the deficiency letter within 1 year of issuance of the deficiency letter, unless within that same timeframe the sponsor requests in writing an extension of time to respond. This request must include the reason(s) for the requested extension and the length of time of the requested extension. FDA will grant all reasonable requests for an extension. In the event FDA denies a request for an extension of time, FDA may consider the designation request voluntarily withdrawn. In the event FDA considers a designation request voluntarily withdrawn, FDA will so notify the sponsor in writing.

(b) FDA will grant the request for orphan-drug designation if none of the reasons described in § 316.25 for requiring or permitting refusal to grant such a request applies.

(c) When a request for orphan-drug designation is granted, FDA will notify the sponsor in writing and will publicize the orphan-drug designation in accordance with § 316.28.

(d) A sponsor may voluntarily withdraw an orphan-drug designation request or an orphan-drug designation at any time after the request is submitted or granted, respectively, by submitting a written request for withdrawal to FDA. FDA will acknowledge such withdrawal in a letter to the sponsor. Any benefits attendant to designation (such as orphan-exclusive approval) will cease once designation is voluntarily withdrawn, from the date of FDA's acknowledgement letter. If a sponsor voluntarily withdraws designation, FDA will publicize such withdrawal in accordance with § 316.28.

[57 FR 62085, Dec. 29, 1992, as amended at 78 FR 35133, June 12, 2013]

§ 316.25 Refusal to grant orphan-drug designation.

(a) FDA will refuse to grant a request for orphan-drug designation if any of the following reasons apply:

(1) The drug is not intended for a rare disease or condition because:

(i) There is insufficient evidence to support the estimate that the drug is intended for treatment of a disease or condition in fewer than 200,000 people

in the United States, or that the drug is intended for use in prevention or in diagnosis in fewer than 200,000 people annually in the United States; or

(ii) Where the drug is intended for prevention, diagnosis, or treatment of a disease or condition affecting 200,000 or more people in the United States, the sponsor has failed to demonstrate that there is no reasonable expectation that development and production costs will be recovered from sales of the drug for such disease or condition in the United States. A sponsor's failure to comply with § 316.21 shall constitute a failure to make the demonstration required in this paragraph.

(2) There is insufficient information about the drug, or the disease or condition for which it is intended, to establish a medically plausible basis for expecting the drug to be effective in the prevention, diagnosis, or treatment of that disease or condition.

(3) The drug is otherwise the same drug as an already approved drug for the same rare disease or condition and the sponsor has not submitted a medically plausible hypothesis for the possible clinical superiority of the subsequent drug.

(b) FDA may refuse to grant a request for orphan-drug designation if the request for designation contains an untrue statement of material fact or omits material information or if the request is otherwise ineligible under this part.

[57 FR 62085, Dec. 29, 1992, as amended at 78 FR 35133, June 12, 2013]

§ 316.26 Amendment to orphan-drug designation.

(a) At any time prior to approval of a marketing application for a designated orphan drug, the sponsor holding designation may apply for an amendment to the designated use if the proposed change is due to new and unexpected findings in research on the drug, information arising from FDA recommendations, or unforeseen developments in treatment or diagnosis of the disease or condition.

(b) FDA will grant the amendment if it finds that the initial designation request was made in good faith and that the amendment is intended to conform